

REMARKS**Status of the Claims**

Claims 1-49 are pending. Claims 33-40 and 44-49 are withdrawn from consideration as being directed to a separate invention. Claims 1-32 and 41-43 are currently under examination.

Amendment to the Claims

Claims 13 and 25 have been amended. Support for the amendments to claims 13 and 25 can be found throughout the specification.

Claim 13 has been amended to correct the misspelling of “thiazolidinedione.”

Representative support for the amendment to claim 25 can be found in figure 2 which discloses various PPAR- γ ligands, wherein their L and M substituents are defined as hydrogens. The amendment to claim 25 does not introduce prohibited new matter.

Objection to Claim

Claim 13 has been objected to because “thiazolidinedione” was misspelled.

Applicants have corrected the spelling of “thizaolidinedione” in claim 13.

Rejection Under 35 U.S.C. § 112, Second Paragraph

A. Claims 1-32 have been rejected under 35 U.S.C. § 112, Second Paragraph, as being indefinite for reciting “susceptible to having.”

Applicants respectfully point out that page 10, paragraph [0044] of the specification provides a definition for “susceptible.” As defined in the specification, the term “susceptible” means that a subject has a predisposition or likelihood of developing an asthma, allergy, or type 1 hypersensitivity. As is known in the art, individuals who are susceptible to these diseases include patients with allergies and type I hypersensitivity reactions that are more likely to develop asthma, families with a history of the disease, as well as those predicted to be susceptible to developing the disease based on genetic or other phenotypic tests. A person having ordinary skill in the art would know that the phrase “susceptible to having a type I hypersensitivity, asthma, or an allergy” does not include “every living subject” that might or might not develop one of these diseases.

It appears that the rejection may be based on the breadth of what is encompassed by the phrase “susceptible to having a type I hypersensitivity, asthma, or an allergy.” Applicants respectfully submit that breadth of a term recited in a claim does not render a claim indefinite (see MPEP 2173.04).

B. Claims 25-32 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for reciting “L and M combine with each other and cooperate jointly to form a linkage and a plurality of salts.”

Claim 25 has been amended to recite that “L is hydrogen and M is hydrogen.” Thus, the claim is not indefinite.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1, 2, 4-24, and 41-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a subject having a type I hypersensitivity, asthma, or allergy comprising administering ciglitazone or other pharmaceutical agents shown in the art to be useful for this purpose, does not reasonably provide enablement for such a method involving any PPAR- γ agonist.

Applicants respectfully point out that the claims as they stand are directed to a method for treating a subject having, or being susceptible to having, a type I hypersensitivity, asthma or an allergy comprising administering a therapeutically effective amount of at least one PPAR- γ agonist or a derivative thereof. Applicants respectfully point out that the specification defines PPAR- γ agonists as compounds that are able to bind to PPAR- γ and to activate the receptor and the claims require that these agonists to be effective in treating type I hypersensitivity, asthma, or allergy. The claims do not encompass any PPAR- γ agonists. The specification provides various examples of PPAR- γ agonists, and the specification discloses assays for determining whether an agonist would be effective in treating type I hypersensitivity, asthma, or allergy (see Examples). Ciglitazone is provided as an example of a thiazolidinedione that is effective in treating human asthma. In addition to showing that ciglitazone is effective in treating asthma, the specification discloses that PGJ2, like ciglitazone, inhibited Th2 cell cytokines IL-4 and IL-5, *in vitro* (see Table 1). This *in vitro* assay is a known assay in this area of research and the results are

considered by those of ordinary skill in the art to be predictive of the success of a corresponding *in vivo* treatment PGJ2 is a non-thiazolidinedione.

As an additional example of PPAR- γ agonist, attached is a reference showing GW1929, a thiazolidinedione, is effective in treating asthma (August *et al.*, 2006). Similar to ciglitazone, GW1929 inhibits the production of Th2 cell immune response and significantly reduced AHR following exposure to allergen.

Accordingly, the specification provides adequate guidance and examples of PPAR- γ agonist for the treatment of type I hypersensitivity, asthma, or allergy. Thus, the claims are enabled by the specification.

Applicants respectfully point out that the initial burden is on the Examiner to provide a reasonable explanation as to why the scope of protection provided by the claim is not adequately enabled by the disclosure. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Moreover, the court in *In re Marzocchi* stated that it is incumbent upon the Patent Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Office Action has not provided any reason to doubt the enablement of the claimed invention. Moreover, the Office Action has not provided a reasonable explanation or evidence establishing the nonenablement of the claims. In the absence of evidence to the contrary, the specification fully enables the claims directed to a method of treating type I hypersensitivity, asthma, or an allergy comprising administering PPAR- γ agonist or derivative thereof.

The Office Action cites the eight Wands factor in considering if a disclosure requires undue experimentation. In the discussion below, Applicants consider these eight factors.

Regarding the nature of the invention and the state of the prior art, Applicants respectfully point out that the various PPAR- γ agonists are known in the prior art. Some of them have been approved for clinical use while others are in Phase II or Phase III clinical trials. Examples of these agonists are shown in the table below.

Agent	Company	Target	Stage
Rosiglitazone	GlaxoSmithKline's Avandia	PPAR- γ agonist	In clinical use
Pioglitazone	Lilly/Takeda's Actos	PPAR- γ agonist	In clinical use
Ciglitazone		PPAR- γ agonist	In clinical use
Metaglidisen	Metabolex	PPAR- γ (partial agonist)	Phase II/III, type 2 diabetes
FK614	Astellas	PPAR- γ (partial agonist)	Phase II, type 2 diabetes
PA-082	Roche	PPAR- γ (partial agonist)	Preclinical, type 2 diabetes

Accordingly, the state of the prior art indicates that PPAR- γ agonists are well known compounds and some have been approved by the FDA for pharmaceutical uses.

Regarding the relative skill of those in the art and the predictability of the art, Applicants respectfully point out that PPAR- γ agonists are well known compounds, as discussed above. Moreover, the specification provides assay for determining whether a PPAR- γ agonist is effective for treating type I hypersensitivity, asthma, and allergies and discloses ciglitazone as an example of PPAR- γ agonist that is useful in treating these diseases. It is within the skill of the artisan to perform either an *in vitro* or *in vivo* assay with a candidate PPAR- γ agonist as taught by the specification and to compare the results with ciglitazone to determine whether the candidate would be effective in treating type I hypersensitivity, asthma, and allergies.

The Office Action alleges that the claims are broad. However, as discussed above, the claims require PPAR- γ agonists that bind to PPAR- γ and to activate the receptor and are effective in treating type I hypersensitivity, asthma, and allergies. The claims do not encompass any and all PPAR- γ agonist.

Regarding the amount of direction or guidance presented and the absence of working examples, the specification provides PGJ2 and ciglitazone and the attached reference of August *et al.* discloses GW1929, as examples of PPAR- γ agonists that are effective in treating asthma. As discussed above, the specification also provides *in vitro* and *in vivo* assays for testing whether a compound is effective in treating asthma.

Applicants respectfully point out that the number of examples is immaterial to enablement. The MPEP 2164.02 states, "Compliance with the enablement requirement does not

turn on whether an example is disclosed.” Moreover, in *Gould*, the court stated that an applicant need not have actually reduced the invention to practice prior to filing. *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ2d 1302, 1304 9Fed. Cir. 1987). Further, the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without undue experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). As discussed above, the application provides sufficient teaching throughout the specification to enable the skilled artisan to practice the invention without undue experimentation.

Regarding the quantity of experimentation, Applicants assert that given the guidance and examples provided by the specification, it would only require routine experimentation to practice the claimed invention. It is well settled that routine experimentation should not be considered as undue in an enablement assessment. As stated in *Ex parte Jackson* and confirmed in *Ex parte Forman*, the court held:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention. Because the present specification provides ample guidance and the experimentation is routine, the claims are in compliance with the section 112 first paragraph requirement.

Ex parte Jackson 217 USPQ 804(Bd. Pat. App. 1982).

Moreover, in *Ex parte D*, the court held,

Parallel to the holding in the *Wands* decision there was a high level of skill in this art at the time the application was filed and the method so needed to practice the invention were well known. . . . [R]outine experimentation may involve rather extensive studies without straying from “undue experimentation.

Ex parte D, 27 USPQ2d 1067 (Bd. Pat App. & Int’f).

Accordingly, the specification enables the claimed invention and it would not require undue experimentation to practice the claimed invention.

Rejection Under 35 U.S.C. § 102 (e)

Claims 1, 2, 4, 5, 8-10, and 41-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Pershadsingh (WO 02/13812).

The claims as they stand are directed to a method for treating a subject having, or being susceptible to having, a type I hypersensitivity, asthma or an allergy comprising administering a therapeutically effective amount of at least one PPAR- γ agonist or a derivative thereof.

Applicants respectfully point out that type I hypersensitivity, asthma, and allergy are caused by elevated Th2 cell responses (see attached references: Walter *et al.* 2001, Webb *et al.* 2000, Wills-Karp *et al.* 1998, and Zhu *et al.* 1999).

Pershadsingh discloses treatment of inflammatory diseases by administering PPAR- γ agonists to suppress Th1-mediated inflammatory cytokines and promote Th1 to Th2 phenotypic transition, leading to treatment or prevention diseases (page 7, lines 25-28). Unlike the present invention, Pershadsingh does not teach administering PPAR- γ agonist to treat diseases that are driven by Th2 immune response. Rather, Pershadsingh teaches administering PPAR- γ agonists to promote Th2 response which would increase the severity of type I hypersensitivity, asthma and allergies. Although Pershadsingh makes the general statement that PPAR- γ agonists can treat asthma and allergies, Pershadsingh cannot anticipate the claimed invention because based on the teachings of Pershadsingh, administering PPAR- γ agonists to patients with asthma and allergies would exacerbate the patients' condition. As discussed in detail in the attached references, asthma and allergies are characterized by elevated Th2 cell responses. Accordingly, Pershadsingh does not teach administering PPAR- γ agonist to treat type I hypersensitivity, asthma, or allergy. Thus, Pershadsingh does not anticipate the claimed invention.

Rejection Under 35 U.S.C. § 103(a)

Claims 3, 6, 7, and 11-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Pershadsingh in view of Adams (U.S. Patent 6,090,836).

The claims recite specific dosages and specific routes of administration of PPAR- γ agonist or a derivative thereof.

As discussed above, Pershadsingh teaches away from treating type I hypersensitivity, asthma, and allergies with PPAR- γ agonists because Pershadsingh teaches administering PPAR- γ

agonists to promote Th2 response which would increase the severity of type I hypersensitivity, asthma and allergies. Thus, Pershadsingh does not teach a method of treating type I hypersensitivity, asthma, or allergy by administering PPAR- γ agonist.

Adams does not cure the deficiencies of Pershadsingh. Adams teaches thiazolidinediones for treating obesity and diabetes. Adams does not teach thiazolidinediones for treating type I hypersensitivity, asthma, or allergy, and Adams does not disclose the specific dosages and routes of administration of PPAR- γ agonist for treating type I hypersensitivity, asthma, or allergy. Accordingly, the teachings of the cited references do not provide motivation to modify the teachings of Pershadsingh and Adams to arrive at the claimed method of administering PPAR- γ agonist to treat type I hypersensitivity, asthma, or allergy. Thus, the cited references do not render the claimed invention obvious.

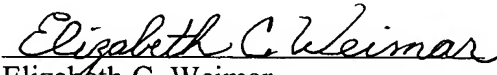
Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should an interview be helpful to further prosecution of this application, the Examiner is invited to telephone the undersigned.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
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